REMARKS

The Examiner is requested to thoroughly consider Applicant's remarks in their entirety.

I. The Claims

Claims 1-21, 23 and 25-40 are pending and claims 17-20, 25, 27, 29, 30, 32 and 36-40 are presently under examination. Claims 1-16 are presently withdrawn as a result of being deemed to be directed to a non-elected inventions and claims 21, 23, 26, 28, 31 and 33-35 are presently withdrawn as being drawn to non-elected species.

Independent claims 17, 18, 25 and 29 have amended herein. Support for the "cellular genome" limitation in each of the independent claims is found in the preambles of claims 17 and 18 themselves, and also in ¶¶21-24 of corresponding U.S. Pub. No. 20040266708 of the originally filed specification. Support for the "thereafter" limitation in amended method claims 17 and 25 is found in the order of the steps in the claims themselves and implicit in the discussion of the originally filed specification, e.g., ¶¶ 124 and 140 of U.S. Pub. No. 20040266708. Support for the "conditionally" limitation is found in ¶10, in the first sentence of ¶82, and in the last sentence of ¶124 of U.S. Pub. No. 20040266708, and in addition, is implicit throughout much of the discussion of the originally filed specification where systems and methods wherein silencing occurs in response to viral infection or other conditions is described.

No new matter has been added by any of the amendments made herein.

II. Claim rejections under 35 U.S.C. §103(a)

Claims 17-20, 25, 27, 29, 30, 32, and 36-40 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,723,765 to Oliver et al. ("Oliver"), in view of both Porter (Trends Genet, 1998, 14: 73-79) and Angell et al (EMBO J, 1997, 76: 3675-3684; "Angell"). (Office Action, ¶4.)

It is noted hat the previous rejection for alleged obviousness over the asserted combination of Oliver in view of Porter was withdrawn in response to Applicant's

amendments and remarks filed March 17, 2008. In the present rejection, the Examiner still relies on Oliver for the teaching of the DNA excision elements (excision system) and Porter for the asserted teaching of RNA silencing to inactivate genes, with the Examiner taking the position that it would be obvious to reduce expression of the repressor protein of the DNA excision system using RNA silencing. The present rejection adds Angell to the combination, on which the Examiner relies for the assertion of the teaching missing in Oliver and Porter that silencing of the repressor protein is by virtue of "providing a repressor having a sequence complementary to a strand of a viral double-stranded RNA and infecting the cell with the double-stranded RNA virus (claims 17, 18, 25 and 29)." Office Action, page 4, l. The Examiner specifically stated that "Angell et al. teach using silencing of transgenes modified such as to include part of the replicating potato virus X (PVX) RNA and infecting the plant cell comprising the transgene with the unmodified PVX." Office Action, page 4, l. 16-19.

The present rejection of the claims is overcome for the following reasons.

The technology of Angell on which the rejection relies in part is dramatically different from that utilized in the presently claimed invention and the present claims have also been amended to even more clearly distinguish the invention with respect to what is taught by Angell, as further explained below.

Angell unambiguously teaches that modified or "unmodified" potato virus X (PVX) may be inserted into the genomic DNA of a plant under control of a plant promoter (CaMV 35S), so that a resulting (regenerated) transgenic plant transcribes from its genome replicative PVX (modified or unmodified).[1] The genomically integrated replicating virus systems are referred to as "amplicons" in Angell. (Angell, e.g., Abstract and page 3675, col. 2, ¶2). In the particular experiment to which the Examiner referred on Angell page 3679, col. 1, last paragraph and FIG. 7, leaf fragments of a plant having a genomically integrated PVX amplicon (that gives rise to "unmodified" PVX dsRNA in

[1] Applicant wishes to point out that the so-called "unmodified" PVX of Angell is actually modified, i.e., unnaturally occurring, since it is inserted between a plant CaMV promoter and 3' nos sequence. This fact also distinguishes the present invention over the prior art, but is not of central relevance to Applicant's main arguments and remarks presented herein. Applicant nevertheless reserves the right to later argue this difference over the prior art in more detail before the Examiner or the Board of Patent Appeals and interferences.

cells) are bombarded (particle bombardment technology) with transient expression constructs having the GUS reporter gene and 3' PVX sequence fragments. (Id.) It was found that the PVX amplicon could silence GUS expression by virtue of the PVX sequences in the GUS reporter construct.

First, independent claims 17 and 18 already specify in each of their preambles that it is the excision construct that is present in and excisable from the **cellular genome** of the plants of these claims. While this limitation already breathes life and meaning into the claim as it clearly distinguishes the claims over the cited prior art, Applicant nevertheless has amended these claims herein to recite the limitation *within the body* of each of claims 17 and 18, and similarly added this language to each of independent claims 25 and 29. In further distinguishing over the prior art by amendment, in independent method claims 17 and 25, the word "**thereafter**" has been added to more clearly specify that the plant having the genomically integrated DNA excision system is first provided, and thereafter unmodified viral dsRNA silences expression of the repressor protein to trigger excision.

Second, in the system of Angell, the plant cells are genetically modified so that PVX is genomically integrated in the plant cells and PVX is transcribed under control of a CaMV 35S promoter in said cells such that a replicating PVX results in the cells. While Angell poses this situation as an "infection" of the cells, it is clear that this type of introduction of virus into the cells is not what is meant by "infecting" by the present application. **¶140 of corresponding Pub. No. 20040266708 clearly refers to "infection" in terms of *entry* into the cell when it states "when particular viruses, virus like agents or other environmental polynucleic acid molecules infect or otherwise enter or are produced in cells as a result of exposure to these agents in the environment." Moreover, independent claim 17 already distinguishes over this aspect of Angell, when claim 17 literally recites "providing the viral double stranded RNA molecule into the plant cell" – this is not what is done in Angell where DNA is introduced into the plant cells and integrated therewith and the cell itself thereafter expresses the viral dsRNA**. Independent claims 18 and 25 similarly distinguish over this aspect of the rejection by specifying in the functional means-for language that the silencing is ***in response*** to the presence of the viral double stranded RNA molecule in the

cell, i.e., not simply caused by the something already present but *in response* to something that occurs.

> (From Present Claim 18) means for causing RNA silencing against the mRNA transcript for the repressor protein *in response to* the presence in the cell of the unmodified viral double stranded RNA having the region of predetermined sequence so that expression of the site specific recombinase is derepressed thereby causing excision of the excisable sequence element

Third, while the system of Angell is interesting and, as pointed in Angell, page 3682, col. 2 (also referred to by the Examiner), teaches that its amplicon constructs are useful for silencing genes in plants, the system of the reference does not have or permit the same functionality of the presently claimed invention, nor does it solve the same problem or have the same advantages as now discussed. The system of Angell provides a plant wherein the cells are expressing active replicating virus from the cellular genomes. If a target having complementarity to the PVX virus enters the cell of Angell, such as the GUS reporter construct of Angell FIG. 7, or is already there (e.g., an endogenous cellular gene), that target will be silenced. The presently claimed invention provides system/methods wherein what will be the target of silencing, i.e., the repressor of the DNA excision system, is integrated (along with the whole excision system) into the plant genome, while the virus that can trigger the silencing that leads to excision is not integrated into the plant cellular genome. As explained previously, by modifying the sequence of the repressor of the excision system to have complementarily to unmodified viral dsRNA sequence this permits **conditional** excision of a preselected DNA sequence from the plant genome in response to infection of the plant cells by the virus having said sequence. This same kind of conditionality is neither taught nor suggested by Angell or the other cited references. **To further facilitate allowance, the independent claims have also been amended herein to explicitly recite the *conditionality* of the excision.** Where "conditionally" now appears in the preambles of the independent claims, it is pointed out that this limitation breathes life and meaning into the claims and should therefore be accorded patentable weight as it is a basis on which the claims are distinguished over the presently cited prior art. (See MPEP 2111.02 Effect of Preamble.)

A conditional system as presently claimed permits certain real world uses that the Angell system does not (neither alone, nor in combination with Porter and Oliver),

namely the present invention provides plants/plant cells whose genome is conditionally altered by infection with a virus that may be used to test or monitor for viral infection, in the environment, as a genomic record in the cells and/or via *activation of a reporter* gene. (See, e.g, ¶¶124 and 140 of corresponding U.S. Pub. No. 20040266708.) In contrast, Angell is just a system where replicating amplicons, which give rise to siRNA, are "always on" in the plant cells. Moreover, while it cannot even be seen whatsoever how Angell could possibly technically permit the functionality of the presently claimed invention, it should also be pointed out that from a safety perspective, it would be completely undesirable to place a plant such as from Angell that genomically drives expression of a replicating virus into the environment or any real world situation, e.g, to avoid recombination with other viruses in the environment. In contrast, the cells of the presently claimed invention do not have genomes driving expression of replicating viruses, nor could it be reasonably concluded that they do.

For the preceding reasons and in view of the instant claim amendments, Angell fails to teach what is missing from the combination of Porter and Oliver alone and, therefore, the asserted combination of Angell, Porter and Oliver does not and cannot result in the presently claimed invention. In addition, the presently claimed invention has functions and provides solutions to problems that are not even remotely suggested by any of the cited references either alone of in combination.

Accordingly, withdrawal of the present rejection of the claims under 35 U.S.C. §103(a) is hereby requested.

III. Conclusion

Pursuant to this paper, Applicant submits that elected claims 17-20, 25, 27, 29, 30, 32 and 36-40 are in condition for allowance, which action is hereby requested.

If, upon considering this paper, any issues are considered to remain, Applicant respectfully requests that the Examiner telephone Applicant at the number below to discuss to discuss the same.

Date: August 18, 2008

Respectfully submitted,

/Paul Diamond/ Reg. No. 48,532

Paul Diamond, Ph.D., Esq.
Attorney and Applicant
Reg. No. 48,532
Customer No. 53255
Telephone: (201) 770-1830